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## **DEPARTMENT OF HEALTH AND HUMAN SERVICES**

### **National Institutes of Health**

#### **Government-Owned Inventions; Availability for Licensing**

**AGENCY:** National Institutes of Health, HHS

**ACTION:** Notice

**SUMMARY:** The inventions listed below are owned by an agency of the U.S.

Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 209 and 37 CFR Part 404 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

**FOR FURTHER INFORMATION:** Licensing information and copies of the U.S.

patent applications listed below may be obtained by writing to the indicated licensing

contact at the Office of Technology Transfer, National Institutes of Health, 6011

Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301-496-

7057; fax: 301-402-0220. A signed Confidential Disclosure Agreement will be required

to receive copies of the patent applications.

## **Use of Antisense Oligodeoxynucleotides (ODNs) for Inhibiting JC Virus (JCV)**

**Description of Technology:** Progressive multifocal leukoencephalopathy (PML) is a rare, fatal demyelinating disease of the brain caused by the polyomavirus JC (JCV) under immunosuppressive conditions. It is pathologically characterized by progressive damage of white matter of the brain by destroying oligodendrocytes at multiple locations. Clinically, PML symptoms include weakness or paralysis, vision loss, impaired speech, and cognitive deterioration. The prognosis of PML is generally poor. No effective therapy for PML has been established. The current strategies to develop a PML therapy focus on blocking viral infection or inhibiting JCV replication. Antisense oligodeoxynucleotides (ODNs) that can block JCV replication and multiplication have been identified and optimized. Use of the ODNs provide a method of inhibiting JCV replication and thereby provide a treatment for PML.

### **Potential Commercial Applications:**

- JCV/PML Therapeutics
- JCV Diagnostics
- JCV Kits

### **Competitive Advantages:**

- Low cost PML therapeutics
- Lower cost JCV diagnostics
- Ease of synthesis

### **Development Status:**

- Pre-clinical

- In vitro data available
- In vivo data available (animal)

**Inventors:** Laura B. Jaeger, Avindra Nath, Eugene O. Major (all of NINDS)

**Intellectual Property:** HHS Reference No. E-547-2013/0 – US Provisional Application No. 61/879,833, filed 19 Sep 2013

**Licensing Contact:** Peter Soukas, J.D.; 301-435-4646; [ps193c@nih.gov](mailto:ps193c@nih.gov)

**Collaborative Research Opportunity:** The National Institute of Neurological Disorders and Stroke is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize anti-JCV antisense cocktails. For collaboration opportunities, please contact Melissa Maderia, Ph.D. at [maderiam@mail.nih.gov](mailto:maderiam@mail.nih.gov) or 240-276-5533.

### **A Novel HIV-1 Anti-HIV and Anti-Retroviral Compound**

**Description of Technology:** The subject invention describes the thioether prodrug that targets the highly conserved nucleocapsid protein 7 (NCp7) of HIV. In contrast to clinically approved anti-retroviral drugs used to treat HIV, the virus is not able to develop resistance to the drug in this invention. In addition, the prodrug is stable at room temperature, crystalline, easily synthesized in two steps on the kilogram scale from inexpensive starting materials, orally bioavailable, and is non-toxic in all animal models investigated to date. There is potential to use the molecule described in the invention as an orally administered systemic drug for the treatment of HIV infection either alone or in combination with other approved anti-retroviral therapies.

Animal safety testing is in process as are efficacy studies.

**Potential Commercial Applications:**

- HIV therapeutics
- Prophylactics
- Topical application

**Competitive Advantages:**

- Does not develop resistance due to the high sequence conservation of the target.
- More stable than thioesters.

**Development Stage:**

- Early-stage
- Pre-clinical
- In vitro data available
- In vivo data available (animal)

**Inventors:** Daniel Appella, Pankaj Kumar, Nathaniel Shank, Matthew Hassink

(all of NIDDK)

**Publications:**

1. Goudreau N, et al. Discovery and structural characterization of a new inhibitor series of HIV-1 nucleocapsid function: NMR solution structure determination of a ternary complex involving a 2:1 inhibitor/NC stoichiometry. J Mol Biol. 2013 Jun 12;425(11):1982-98. [PMID 23485336]
2. Ouyang W, et al. Probing the RNA Binding Surface of the HIV-1 Nucleocapsid Protein by Site-Directed Mutagenesis. Biochemistry 2013;52(19):3358-68. [PMID 23594178]

**Intellectual Property:** HHS Reference No. E-539-2013/0 – US Provisional Application No. 61/874,182 filed 05 September 2013

**Related Technologies:** HHS Reference No. E-177-2010 family which is abandoned. However, the subject compound was described in PCT Application No. PCT/US2011/039909 (E-177-2010/0-PCT-02).

**Licensing Contact:** Sally H. Hu, Ph.D., M.B.A.; 301-435-5606;  
[hus@mail.nih.gov](mailto:hus@mail.nih.gov)

**Collaborative Research Opportunity:** The NIDDK Technology Advancement Office is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this anti-retroviral drug that targets the nucleocapsid protein 7 (NCp7). For collaboration opportunities, please contact Marguerite J. Miller at [Marguerite.Miller@nih.gov](mailto:Marguerite.Miller@nih.gov) or 301-496-9003.

### **Mouse Model for Methylmalonic Acidemia, an Inherited Metabolic Disorder**

**Description of Technology:** Methylmalonic Acidemia (MMA) is a metabolic disorder affecting 1 in 25,000 to 48,000 individuals globally. MMA is characterized by increased acidity in the blood and tissues due to toxic accumulation of protein and fat by-products resulting in seizures, strokes, and chronic kidney failure. About 60% of MMA cases stem from mutations in the methylmalonyl CoA mutase (MUT) gene encoding a key enzyme required to break down amino acids and lipids. Previous efforts to develop mice with null mutations in MUT have been unsuccessful, as such mutations result in neonatal death.

The inventors have developed the first transgenic mouse model available for the long-term study of Mut deficiency, in which low level liver-specific expression of the MUT enzyme confers rescue from neonatal lethality and replicates induction of the severe renal symptoms consistent with human MMA. This model could serve as a valuable research tool for designing treatments for MMA renal disease or a platform for pre-clinical toxicology screening of compounds with potential renal side effects.

**Potential Commercial Applications:**

- Model for examining renoprotective antioxidants or treatments for kidney failure resulting from drug toxicity, mitochondrial dysfunction, environmental exposure, or aging.
- Used in investigating renoprotective effects of nutritional supplements from drugs known to cause kidney damage.
- Used in discovery of MMA biomarkers.

**Competitive Advantages:** The model system provides a relatively non-invasive means of assessing the efficacy of renal-targeted therapies of all classes and biological types (gene therapy, small molecules, nutritional supplements, repurposed drugs).

**Development Stage:**

- Early-stage
- Pre-clinical
- In vitro data available
- In vivo data available (animal)

**Inventors:** Charles P. Venditti and Eirini Manoli (NHGRI)

**Publication:** Manoli I, et al. Targeting proximal tubule mitochondrial dysfunction attenuates the renal disease of methylmalonic acidemia. Proc Natl Acad Sci U S A. 2013 Aug 13;110(33):13552-7. [PMID 23898205]

**Intellectual Property:** HHS Reference No. E-285-2011/1 – Research Material. Patent protection is not being pursued for this technology.

**Licensing Contact:** Vince Contreras, Ph.D.; 301-435-4711;  
[vince.contreras@nih.gov](mailto:vince.contreras@nih.gov)

**Collaborative Research Opportunity:** The National Human Genome Research Institute, Organic Acid Research Section, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize renotherapeutic or renoprotective small molecules, gene and/or cell therapies to treat MMA. For collaboration opportunities, please contact Charles P. Venditti, M.D., Ph.D. at [venditti@mail.nih.gov](mailto:venditti@mail.nih.gov) or 301-496-6213.

### **Reporter Plasmid to Identify Cancer Stem Cells**

**Description of Technology:** Scientists at the NIH have developed a research tool, an efficient lentiviral plasmid to visualize and purify cancer stem cells, which is useful for screening compounds that specifically kill or inhibit cancer stem cells. Cancer stem cells are a minority population of cells that initiate and sustain tumors. These cells are resistant to therapy and may cause tumors to recur after curative treatment. Current therapies generally do not target cancer stem cells. The key feature of the plasmid is a reporter system that only detects cells expressing the core stem cell transcription factors Sox2 and Oct4. The plasmid can identify the putative cancer stem cell population

through the expression of fluorescent or luminescent proteins and has the potential to advance new therapies.

**Potential Commercial Applications:**

- Laboratory tool to visualize, quantify and purify cancer stem cells.
- Research tool to monitor cancer stem cells in transplanted tumors in vivo.
- Research tool to identify cancer stem cells in high through-put screening of libraries for compounds that specifically inhibit or kill cancer stem cells.
- Research tool to optimize therapeutic regimens in preclinical models
- Potential to support precision medicine approach by screening therapeutics for efficacy against cancer stem cells in patient-derived xenografts.

**Competitive Advantages:**

- Efficient visualization of cancer stem cells by functional property rather than by use of highly variable cell surface markers
- Flexible modular Gateway cloning technology allows constructs with alternative reporters to be readily generated
- Approach is independent of cell-of-origin of tumor
- Cancer stem cell behavior can be monitored in real-time

**Development Stage:**

- Pre-clinical
- In vitro data available
- In vivo data available (animal)

**Inventors:** Lalage Wakefield and Binwu Tang (NCI)

**Publication:** Manuscript under review. Text available on request.



**Intellectual Property:** HHS Reference No. E-141-2011/0 – Research Tool.

Patent protection is not being pursued for this technology.

**Licensing Contact:** Eggerton Campbell, Ph.D.; 301-435-5282;

[eggerton.campbell@nih.gov](mailto:eggerton.campbell@nih.gov)

**Collaborative Research Opportunity:** The National Cancer Institute, Laboratory of Cancer Biology and Genetics, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize a cancer stem cell reporter construct for use in drug screens and therapy selection. For collaboration opportunities, please contact John D. Hewes, Ph.D. at [hewesj@mail.nih.gov](mailto:hewesj@mail.nih.gov).

### **AAV-Aquaporin-1 Gene Therapy for Sjögren's Syndrome**

**Description of Technology:** Sjögren's syndrome is a chronic inflammatory disease affecting over 2 million Americans, whereby moisture-producing glands are attacked by the body's immune system. The disease is marked by disabling dryness of the mouth and eyes as well as fatigue and pain. Researchers at the National Institute of Dental and Craniofacial Research have developed a therapy that alleviates xerostomia in an animal model of Sjögren's syndrome. This technology consists of local delivery of adeno-associated virus (AAV) mediated aquaporin-1 (AQP1) fusion protein to salivary glands. Using a murine model that mimics Sjögren's dry mouth symptoms, it was discovered that treatment restored salivary fluid movement upon expression of AQP1. Targeted delivery of the AAV-AQP1 system makes this invention a novel and potential

long-term therapeutic for restoration of exocrine gland function and prevention of xerostomia-associated pain associated with Sjögren's syndrome.

**Potential Commercial Applications:** Prevention of dry mouth (xerostomia) associated with salivary gland dysfunction in patients with Sjögren's syndrome.

**Competitive Advantages:**

- AAV gene transfer to salivary glands is highly efficient.
- AAV-AQP1 promotes de novo salivary flow.

**Development Stage:**

- Pre-clinical
- In vitro data available
- In vivo data available (animal)

**Inventor:** John (Jay) Chiorini (NIDCR)

**Intellectual Property:** HHS Reference No. E-139-2011/1 –US Provisional Application No. 61/695,753 filed 31 August 2012; PCT Application No. PCT/US13/57632 filed 30 August 2013

**Related Technologies:**

- HHS Reference No. E-179-2005/0 – US Patent No. 8,283,151 issued 09 October 2012
- HHS Reference No. E-087-2011/0 – US Provisional Application No. 61/476,168 filed 15 April 2011
- HHS Reference No. E-127-1998/0 – US Provisional Application No. 60/087,029 filed 28 May 1998; US Patent No. 7,479,554 issued 20 January 2009; US Patent No. 6,984,517 issued 10 January 2006

- HHS Reference No. E-142-2011/0 – US Provisional Application No. 61/477,523

filed 20 April 2011

**Licensing Contact:** Vince Contreras, Ph.D.; 301-435-4711;

[vince.contreras@nih.gov](mailto:vince.contreras@nih.gov)

**Collaborative Research Opportunity:** The National Institute of Dental and Craniofacial Research, AAV Biology Section, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize AAV-Aquaporin-1 Gene Therapy for Sjögren's. For collaboration opportunities, please contact David Bradley at [bradleyda@nidcr.nih.gov](mailto:bradleyda@nidcr.nih.gov).

December 2, 2013

Date

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Richard U. Rodriguez,  
Director  
Division of Technology Development and Transfer  
Office of Technology Transfer  
National Institutes of Health

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